

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
12 May 2005 (12.05.2005)

PCT

(10) International Publication Number  
WO 2005/042476 A3

(51) International Patent Classification<sup>7</sup>: C07C 315/00, 323/00, A61K 31/19, 31/215, 31/195

(21) International Application Number: PCT/US2004/034374

(22) International Filing Date: 18 October 2004 (18.10.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 60/513,284 22 October 2003 (22.10.2003) US

(71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ARRUDA, Jeanne, M. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). MUÑOZ, Benito [CA/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). STEARNS, Brian, A. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

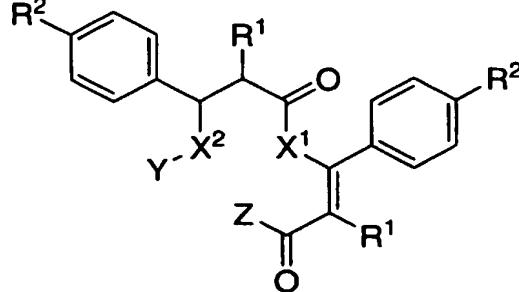
Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

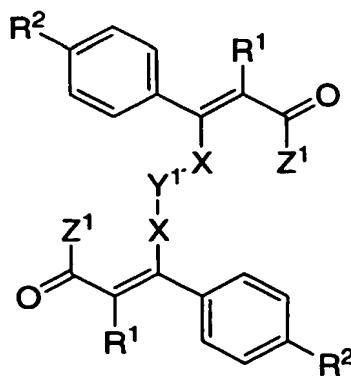
(88) Date of publication of the international search report: 9 June 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PRODRUGS OF DIARYL-2-(5H)-FURANONE CYCLOOXYGENASE-2 INHIBITORS



I



II

WO 2005/042476 A3

(57) Abstract: The invention encompasses the novel compounds of Formula (I) and Formula (II), which are prodrugs that convert *in vivo* to diaryl-2-(5H)-furanones useful in the treatment of cyclooxygenase-2 mediated diseases. These prodrugs are far more soluble in aqueous media than the active agents into which they convert, *in vivo*. As such compounds of Formula (I) and (II) are advantageous for, among other things intravenous administration. The invention also encompasses certain pharmaceutical compositions and methods for treatment of cyclooxygenase-2 mediated diseases comprising the use of compounds of Formula (I) and Formula (II).